1105 HOW VARICELLA VACCINE WORKS: AN APPRAISAL WITH MONOCLONAL ANTIBODIES. Charles Grose University of Iowa, Department of Pediatrics, Iowa City, Iowa 52242

Studies with the live attenuated strain (VZV-Oka) of varicella zoster virus vaccine demonstrate a high degree of efficacy in protecting children with leukemia from contracting wild-type chickenpox. The purpose of this study was to determine which were the most important immunogenic proteins of VZV-Oka and to identify neutralization epitopic sites. Prior investigations of the immune response to wild type chickenpox indicate that the predominant antibody response is directed against the major viral glycoproteins. In order to evaluate VZV-Oka, murine monoclonal antibodies were produced against its viral glycoproteins. Specificities of antibodies were determined by techniques of immunoprecipitation and immunoblotting. By these studies we divided the glycoproteins into three groups: (1) gp118 (2) gp98/gp62/gp45 and (3) gp140/gp66. Biologic activity of each antibody was assayed by the technique of plaque reduction. A panel of antibodies against VZV gp118 were shown to possess marked neutralization activity (with titers to 1:40,000) against homologous and heterologous VZV strains. A titer of this magnitude indicates that glycoprotein gp118 of VZV-Oka harbors a major neutralization epitope. Glycoproteins gp140/gp66 also contained a complement-independent neutralization epitope but none was detected on the gp98 complex. These analyses with monoclonal antibodies define biologically important antigenic sites of VZV-Oka and suggest a role for the same glycoproteins in any future subunit vaccine.

†1106 CHEMICAL, SEROLOGICAL, AND FUNCTIONAL ANALYSES OF PURIFIED H. INFLUENZAE PILI. Nicholas Guerina, Solomon Langermann, Gary Schoolnik, Donald Goldmann. Harvard Medical School, Children's Hospital, Dept. of Pediatrics, Boston, MA. and Div. of Infectious Diseases, Stanford Univ. Med. Center, Palo Alto, CA

We have purified and characterized pili from clinical isolates of H. influenzae. Pilus preparations were highly pure by multiple criteria and consisted of intact rods composed of a 25K dalton subunit. Amino acid sequence analysis revealed a high degree of N-terminus homology with E. coli type 1 and P pili, suggesting a common gene ancestry. Purified pili hemagglutinated human type O RBCs and were used in a microtiter plate assay incorporating synthetic saccharides to identify the pilus receptor. Pilus receptor binding by purified pili and piliated H. influenzae was blocked by homologous and heterologous anti-pilus antiserum. Receptor binding inhibition was pilus-specific antibody concentration dependent, but was observed even with antisera showing <10% cross-reactivity. Purified pili were highly immunogenic, with homologous ELISA titers ranging from 3×10^5 to 10^6. Heterologous titers ranged from 2% - 100% homologous titers with 40% of the strains tested showing >50% cross-reactivity. Pili from type b and non-typable strains were serologically, chemically and functionally similar. H. influenzae and E. coli P pili were serologically related but differed in receptor specificity suggesting functional divergence. These results indicate that there are a relatively small number of major antigenic groups of H. influenzae pili which may be important to the development of a pilus vaccine.

●1107 RIBAVIRIN (RIB) THERAPY OF RESPIRATORY SYNCYTIAL VIRUS (RSV) INFECTION IN INFANTS WITH CARDIOPULMONARY DISEASE. Caroline B Hall, John T McBride, Christine L Gala. University of Rochester Medical Center, Department of Pediatrics, Rochester, New York.

Aerosolized Rib has appeared beneficial in the treatment of RSV pneumonia in selected normal infants in a previous study. We have since evaluated Rib therapy of RSV lower respiratory tract infection (LRI) in infants with underlying cardiopulmonary disease to determine its efficacy and safety in such high risk infants. 22 infants with RSV LRI were studied in '83-84 in a randomized double-blind manner to receive aerosolized Rib (12) or placebo (10) (water). An additional 20 infants with life-threatening illness were not randomized, but treated with Rib. 26 infants (10 randomized, 16 non-randomized) had bronchopulmonary dysplasia or congenital heart disease. The 22 randomized infants received Rib or placebo for 21 hrs/d. for 3-8 days (mean=5d) and were matched in age (15wks), sex, underlying disease, duration of illness before therapy and severity of illness on admission. At start of therapy Rib infants had greater illness severity scores by double blind exam than placebo pts (p.06). But Rib pts showed faster and greater improvement by d.3 ($p<.01$), d 4 and end of Rx ($p=.002$). Arterial oxygen saturations determined daily also improved more in Rib pts ($p<.05$). Daily quantitation of viral shedding showed significantly lower titers in Rib pts on d 5,6 ($p<.03$) and % of Rib pts still shedding was less on d 5 ($p=.04$) & d.6 ($p=.007$). The 20 non-randomized infants (mean age 25 wks) were treated with Rib for 4-22 days. 15(75%) required respirators. Viral shedding ceased in all ≤ 6 d from start of Rib. All but one recovered from acute infection; 3 others died > 1 month later.

In all 42 infants Rib as an aerosol was administered safely & without signs of toxicity. Administration of Rib through a respirator required careful monitoring but was without adverse effect. These findings suggest Rib is beneficial and may be safely administered to infants with cardiopulmonary disease at high risk for severe RSV infection.

●1108 BACTERIOPHAGE HYALURONIDASE (BHase) ANTIBODY RESPONSE IN ACUTE GLOMERULONEPHRITIS (AGN) FOLLOWING GROUP A STREPTOCOCCAL (GAS) INFECTION. SA Halperin, ED Gray, P Ferrieri, EL Kaplan, LW Wannamaker, University of Minnesota Medical School, Department of Pediatrics, Minneapolis, Minnesota.

The factors contributing to the development of AGN following infection with a nephritogenic GAS are not well understood. To test the hypothesis that lysogeny with a temperate bacteriophage might confer nephritogenicity, 283 sera from 69 children were examined for presence of IgG and IgM antibodies to M 49 GAS BHase using an enzyme immunoassay (ELISA). Patients were classified as follows: 1) NAGN, 21 patients without AGN, non-nephritogenic GAS infection; 2) NAGN-M49, 31 patients without AGN, nephritogenic M 49 GAS infection; 3) AGN-M49, 15 patients with AGN, M 49 GAS infection; 4) AGN-M57, 2 patients with AGN, M 57 infection.

The maximum IgG titer change ($\log_{10}$) was greatest in AGN-M49 (0.71), and was significantly higher than in NAGN-M49 (0.45, $p=0.016$) or NAGN (0.15, $p<0.001$). NAGN-M49 also had significantly greater titer changes than NAGN ($p<0.001$). Both AGN-M49 (0.25) and NAGN-M49 (0.21) had significantly greater maximum IgM titer changes than NAGN (0.10, $p=0.004$, $p<0.001$ respectively), but were not different from each other ($p=0.46$). Magnitude of antibody titer change (>0.3 log change) differed significantly between individuals infected with M 49 GAS versus other GAS serotypes whether or not AGN was present; highest antibody titer changes (>0.7 logs), however, were seen following AGN. It was concluded that, despite significant rises in IgG and IgM antibody to BHase, antibody response could not be used to investigate the relationship between lysogeny and AGN due to its presence in both patients with and without AGN following M 49 GAS infection.

1109 BLOOD ENDOTOXIN DETERMINATIONS IN THE EVALUATION OF FEBRILE NEUTROPENIC PATIENTS. Ada Hass, Alexander C. Hyatt and David S. Hodes. The Mt. Sinai School of Medicine, Dept. of Pediatrics, New York, New York

An increasing number of febrile episodes in neutropenic patients are never explained etiologically. As a result many such episodes are managed by purely empiric therapy. We wished to explore the hypothesis that some of these episodes might be explained by endotoxemia in the absence of bacteremia. To test this possibility we employed a highly sensitive endotoxin assay which is based on the chromogenic release of p-nitroaniline from a peptide-linked form in the presence of endotoxin (ET) and limulus lysate. This assay, as developed by Seikagaku Kogyo Co, Tokyo, is capable of detecting circulating ET in pg/ml concentrations.

We found that circulating ET was not detectable in normal patients. By contrast circulating ET in concentrations ranging from 20-200 pg/ml was found in neutropenic patients suffering febrile episodes. Endotoxemia was found in the absence of bacteremia and, on occasion, the detection of endotoxemia preceeded the onset of demonstrable gram negative septicemia by several days.

We believe that the sensitive detection of circulating ET can be a valuable adjunct in the assessment of the febrile neutropenic patient, and we are currently extending our studies.

1110 URINARY TRACT INFECTIONS IN CEREBRAL PALSY PATIENTS. Joan M. Hellquist, Ross E. McKinney, Jr., Gordon Worley. Duke University Medical Center, Department of Pediatrics, Durham, North Carolina

100 patients admitted to a children's rehabilitative hospital with a diagnosis of cerebral palsy had a careful review of their history of urinary tract infections (UTIs), a complete physical examination, and a screening urine culture (Uricult). Patients with >10,000 colonies/ml of the Uricult had their result confirmed by a repeat culture. 19 patients had a history of previous UTI(s), 63% of whom also had at least some daytime urinary incontinence. Of the 81 patients without a known previous UTI, 60% were incontinent of urine. 92 patients had Uricults obtained. 3 of these studies had >10,000 colonies/ml, all of which were confirmed on restudy. However, one of these results probably reflected contamination, giving a prevalence of UTIs of 2.2% at admission. Of the 89 patients with negative Uricults, (≤10,000 colonies/ml), 12 (13.5%) were known to have received antibiotics within the previous 7 days, 23 (25.8%) within the last 3 months. An antibiotic history was not available for 13 (7 day history) and 29 (3 month history) children, which means that the antibiotic use may be even higher than the rates obtained. In summary, screening Uricults done on 92 of 100 consecutive admissions uncovered only 2 UTIs in a population of children with cerebral palsy, a rate similar to the general population. However, the prevalence in this study may be lower than the prevalence of UTIs in the population of children with cerebral palsy at large due to the high level of antibiotic usage in the group studied. A history of UTIs was found in 19%.